REMARKS

In view of the following remarks, the Examiner is requested to withdraw the rejections and allow Claims 1-8, 11-18 and 21-23, the only claims pending and currently under examination in this application.

Withdrawal of Rejections

The Applicant thanks the Examiner for withdrawing the prior rejections under 35 U.S.C 101, 35 U.S.C 112 first and second paragraphs and 35 U.S.C 103.

Formal Matters

The specification has been amended at lines 11 and 12 of page 20 to specify that step e. of the algorithm therein indicates that if S is greater than H, this is the best region so far; set B to start at C and end at this marker; set H to S. The Applicants have amended the specification thus to correct an obvious typographical error since the clear intention of the preceding discussion is that the algorithm find "a consecutive region with the highest sum in an array of numbers" (specification, page 9, line 22). The amended algorithm is now consistent with the description in the specification and, as such, adds no new matter.

Claims 1, 11 and 21 have been amended to specify analyzing the actual and estimated genotype data to find a region in genomes of the affected people or a region in genomes of parents of the affected people. Support for this amendment can be found in the specification at page 15, line 10 which states:

> Actual genotype data also can be determined for the parents of affected persons.

Claims 1, 11 and 21 have further been amended to specify determining a set of scores under various assumptions for each of the markers in the actual and estimated genotype data relative to each person for which actual genotype data was determined, with the set of scores for each marker including at least first scores generated to

determine probabilities of observing each marker given autozygosity with the founder and second scores generated to determine probabilities of observing each marker given absence of autozygosity with the founder. Support for this amendment can be found in the specification at page 17, lines 1-3 which states:

> The calculations in that row are performed to determine probabilities of observing that marker given various types of autozygosity with the founder and also the probability of observing that marker in the absence of autozygosity.

Claims 1, 11 and 21 have further been amended to specify merging the set of scores for each marker to produce a merged score for each marker, in which the step of merging includes computing for each of the markers a ratio of the first scores to the second scores, where each merged score indicates at least in part a statistical distinction between whether the marker is autozygous and whether the marker is not autozygous. Support for this amendment can be found in the specification at page 17, line 18 through page 19, line 3, equations from which are reproduced below:

> More formally, if O is a set of genotype measurements believed to come from a single founder (i.e., genotypes of persons affected by the disease or trait under study), o is one of the genotypes in O, Pr(o | autozygous i) and Pr(o | not autozygous) come from the table in Figure 5 (which in turn comes from the table in Figure 4), and i is an index of different possible alleles at each marker, then
>
> $$\Pr(O \mid \text{autozygous } i) = \prod_{o \in O} \Pr(o \mid \text{autozygous } i),$$
>
> $$\Pr(O \mid \text{autozygous}) = \sum_{i} p_i \Pr(O \mid \text{autozygous } i), \text{ and}$$
>
> $$\Pr(O \mid \text{not autozygous}) = \prod_{o \in O} \Pr(o \mid \text{not autozygous}).$$

Fourth, the ratio of Pr(O | autozygous) to Pr(O | not autozygous) is computed for each marker. Preferable, a log base 10 is taken of each ratio. More formally:

$$\text{Marker Score} = \log_{10} [\Pr(O \mid \text{autozygous}) / \Pr(O \mid \text{not autozygous})]$$

The resulting score is comparable to a LOD score obtained through different types of analysis such as genetic linkage or sib pair analysis.

As shown in the above excerpt, the specification teaches calculating the likelihood of observing the actual measured value for the marker given that the marker is autozygous, calculating the likelihood of observing the actual measured value for the marker given that the marker is not autozygous and comes independently from the overall population distribution, and taking the ratio of the first likelihood to the second.

Specifically, the cited passage teaches: computing for each of the markers (*"i is an index of different possible alleles at each marker"*) a ratio of the first scores to the second scores (*"the ratio of Pr(O | autozygous) to Pr(O | not autozygous) is computed for each marker"*) where each merged score (*page 17, line 18: "Next, in step 34, the scores are merged"*) indicates at least in part a statistical distinction between whether the marker is autozygous and whether the marker is not autozygous (*please see page 18, lines 1-5 and page 18, lines 7-11 defining the terms Pr(O | autozygous) and Pr(O | not autozygous) as used in the above ratio calculation).*

Claims 1, 11 and 21 have further been amended to specify examining the merged scores to determine one or more contiguous regions of markers by locating a statistically significant gap in sums of merged scores for non-overlapping contiguous regions of markers and in which contiguous regions of markers having scores above the gap are determined to be the one or more contiguous regions of markers. Support for

this amendment can be found in the specification at page 19, line17 through page 21, line 6 and in Original Claims 10 and 20, which state:

> 10 (20). A method as in claim 9 (19), further comprising the step of locating a statistically significant gap in the scores for non-overlapping regions, wherein regions having scores above the gap are determined to be the one or more additional regions of markers.

Claims 1, 11 and 21 have further been amended to specify storing the at least one contiguous region likely to contain a recessive allele associated with the genetic disease or trait to a computer-readable memory. Support for this amendment can be found in the specification at page 22, lines 3-9, which state:

> Those skilled in the art would recognize, after perusal of this application, that embodiments of the invention may be implemented using one or more general purpose processors or special purpose processors adapted to particular process steps and data structures operating under program control, that such process steps and data structures can be embodied as information stored in or transmitted to and from memories (e.g., fixed memories such as DRAMS, SRAMs, hard disks, caches, etc., and removable memories such as floppy disks, CD-ROMs, data tapes, etc.)

The remaining amendments to the claims are to make sure that, where appropriate, dependent claims terms have appropriate and clear antecedent basis, to correct typographical errors, and to correct errant dependencies.

Because these amendments add no new matter, entry thereof by the Examiner is respectfully requested.

Sequence Rules Compliance

The Applicants have provided a paper copy and a computer-readable form of Sequence Listing and a statement under 37 CFR 1.821(f) to comply with the requirements of 37 CFR 1.821 through 1.825.

Claim Rejections – 35 USC § 112

Claims 1-8, 10-18, and 20-23 are rejected under 35 U.S.C. 112, first paragraph, as allegedly failing to comply with the written description requirement. It is alleged that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Specifically, the Examiner states that amendment to independent claims 1, 11, and 21 to include the limitation "examining said marker scores to determine one or more contiguous regions of markers with a high sum of marker scores" finds insufficient support in the specification.

Applicants submit that the instant claims are now directed to, *inter alia*, determining a set of scores under various assumptions for each of the markers in the actual and estimated genotype data relative to each person for which actual genotype data was determined, with the set of scores for each marker including at least first scores generated to determine probabilities of observing each marker given autozygosity with the founder and second scores generated to determine probabilities of observing each marker given absence of autozygosity with the founder, and merging the set of scores for each marker to produce a merged score for each marker, in which the step of merging includes computing for each of the markers a ratio of the first scores to the second scores, where each merged score indicates at least in part a statistical distinction between whether the marker is autozygous and whether the marker is not autozygous .

The Applicants respectfully submit that the claims as written find specific support on page 17, line 1 through page 19, line 3. Accordingly, it is believed that this aspect of the rejection has been adequately addressed.

The Examiner further alleges that there is insufficient support in the specification for the calculation of multiple runs for "one or more" contiguous regions because page 19 of the specification describes a run of high scores and a contiguous run of scores with the highest sum in the singular.

The Applicants respectfully disagree, and submit that support for the storage of multiple values in matrices is found throughout the specification. Figure 3 plainly states that all the steps in the claimed method may be implemented on a computer network, website, etc. and that scores can be stored in arrays for easier computation. The paragraph spanning pages 14 and 15 states that arrays are particularly useful for handling genotype data and scores. The ordinarily skilled artisan thereby understands that wherever the goal of producing multiple values or results is desirable, matrices and the means for storing and accessing them can be used according to methods that are well known in the art.

Specifically with regard to algorithms for determining runs of high scores, the final paragraph of page 20 and first paragraph of page 21 state:

> High-scoring runs besides the highest-scoring run also can be of interest. For example, the next-highest runs determined using the foregoing technique might be of interest. A statistically significant jump or gap in scores between high-scoring runs and low-scoring runs could be used to select interesting regions. For example, if the highest scoring run has a score of 20, the next highest non-overlapping run has a score of 18 or 19, and the next nearest highest non-overlapping run has a score of 6, then the regions corresponding to scores of 18 or 19 and 20 might be of interest.

> In addition, other techniques for finding runs of high scores (but not necessarily the highest run) can be used. In one such embodiment, the region of markers that has the high run of merged scores is found by computing all sums of a predetermined fixed number of adjacent elements in the array and comparing the sums. For example, if the total array of merged scores has 100 scores, the sums of all 10 score runs could be computed, resulting in 91 sums that could then be compared. Other techniques can be used.

The specification thereby teaches that multiple high-scoring runs may be of interest and, moreover, provides a specific example in which at least 4 iterations of determining a run of high scores are performed, and a second specific example in which 10 runs are performed and the results compared.

As such, the specification (A) clearly teaches the use of stored values and matrices where needed, and (B) clearly teaches the goal of conducting multiple runs of the exemplified algorithms to determine multiple runs of high scores and comparing the results. Accordingly, the Applicants submit that upon reading the claims in light of the specification, it is clear to the ordinarily skilled artisan that the specification amply supports the recited "one or more" regions.

The Examiner further states that the disclosed exemplified algorithm on page 20 of the instant specification does not calculate a sum of marker scores because the final step (e) sets S to H, thereby returning a value of 0 at any number of iterations.

The Applicants have amended the specification to correct this obvious typographical error, since, as the Examiner kindly points out, the clear intention of the preceding discussion is that the algorithm find "a consecutive region with the highest sum in an array of numbers" (specification, page 9, line 22). The final step (e) has been amended by swapping the terms H and S, and the algorithm now functions according to the stated intention of the specification.

The Examiner further alleges that the amendment of the independent claims to recite the limitation "reporting said at least one contiguous region likely to contain a recessive allele associated with said genetic disease or trait to a user of said computing device" is not supported by the specification.

The Applicants submit that the instant claims now recite storing said at least one contiguous region likely to contain a recessive allele associated with the genetic disease or trait to a computer-readable memory. The Applicants submit that the instant amendments find specific support on page 22, lines 7-9 of the specification.

The Examiner additionally cites dependent claims 6-8, 10, 16, 17 and 20 as deficient for the reasons as applied to the claims cited above. The Applicants reiterate the arguments made above with respect to the dependent claims and, where necessary, have amended the cited claims to be consistent with any amendments to claims from which they depend.

In view of the foregoing discussion, it is believed that the rejection has been adequately addressed. Reconsideration and withdrawal of the rejection are respectfully requested.

Claims 1-8, 10-18, and 20-23 are rejected under 35 U.S.C. 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Specifically, the Examiner states that amendment of independent claims 1, 11, and 21 to include the phrase "actual and estimated" makes the claims indefinite since the claims do not require that the actual genotype data come from genomes of affected

people and it is therefore unclear how one could have markers in the actual genotype data when the actual genotype data is not obtained from affected people.

Without in any way agreeing with the position of the Office and solely in order to expedite prosecution of the application, the Applicants have amended the instant claims to recite analyzing the actual and estimated genotype data to find a region in genomes of the affected people or a region in genomes of parents of the affected people, and as such respectfully request reconsideration and withdrawal of the rejection.

The Examiner further alleges that amendment of Claims 1, 11 and 21 to include the phrase "high sum of marker scores" renders the claims indefinite because the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The Applicants respectfully disagree.

The Applicants submit that the instant claims are now directed to a method including examining the merged scores to determine one or more contiguous regions of markers by locating a statistically significant gap in sums of merged scores for non-overlapping contiguous regions of markers and in which contiguous regions of markers having scores above the gap are determined to be the one or more contiguous regions of markers.

As such, the Applicants submit that methods of ascertaining the requisite degree are recited in the claims in a manner readily understood by the ordinarily skilled artisan.

Moreover, the Applicants respectfully point out that the mere fact that individual consideration may be required to set a sum cutoff for a given analysis does not render the instant claims indefinite. The Office is reminded that the breadth of a claim is not to be equated with indefiniteness. *In re Miller*, 441 F.2d 689, 169 USPQ 597 (CCPA 1971).

In other words, simply because a range of differences can be employed in the claimed methods does not mean that the instant claim as written is indefinite.

The Applicants submit that, as cited above, page 20, lines 17-23 of the specification provides a specific example in which a statistically significant gap is noted between the contiguous score values in a set of runs (i.e., 18, 19, 20) and the remainder of scores (i.e. the next highest score for a non-overlapping run is 6). Other methods are also discussed (page 21), and one of skill readily understands that similar statistical methods as known in the art can be used to determine a region of markers which is of interest, depending upon the range of values obtained by a given set of runs.

Moreover, the Applicants respectfully submit that the presence of such teaching in the specification is substantiated by the dependent Claims 7, 8, 17, and 18, as well as original Claims 9 and 19, which recite additional details of such methods, and which claims have not specifically been cited by the Office for failure of support by the specification.

Accordingly, the Applicants submit that the scope of the instant claims is clear and the language definite, particularly in light of the specification. Reconsideration and withdrawal of this aspect of the rejection are respectfully requested.

The Examiner states that the limitation of Claims 4 and 14 reciting "said marker score for a marker" is unclear because a marker has multiple marker scores. The Applicants respectfully submit that since the instant claims now recite "each said merged score for a marker," this rejection is moot.

The Examiner states that the limitation of Claims 10 and 20 reciting "said sums" has insufficient antecedent basis in the claims from which they depend. Since the Applicants have canceled the instant claims, this rejection is now moot.

In view of the foregoing discussion, it is believed that the rejection has been adequately addressed. Reconsideration and withdrawal of the rejection are respectfully requested.

CONCLUSION

Applicants submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone Bret Field at (650) 327-3400.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-1078, order number 10050845-1.

Respectfully submitted,

Date: June 18, 2007

By: _____
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